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ARMY PROJECT ORDER NO: 91PP1801

TITLE: MAINTENANCE SUPPORT OF A FIELD STATION IN SIERRA LEONE, WEST AFRICA

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The purpose of this addendum is to report the laboratory testing and data analysis results referenced in the last section of May 1, 1992, final report. The development of additional diagnostic tests and testing of 91 sera are described in the Final Analysis section of this addendum.

This addendum is a summary of the investigations of suspect Lassa fever cases completed since submission of the final report dated May 1, 1992.

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Final Report

Memorandum of Understanding
(Army Project Order 91PP1801)

MAINTENANCE SUPPORT OF A FIELD STATION IN SIERRA LEONE, WEST AFRICA FOR LASSA FEVER INVESTIGATIONS

Supplemental Final Report

March 8, 1994

Purpose of Supplemental Report: The purpose of this addendum is to report the laboratory testing and data analysis results referenced in the last section of the May 1, 1992 report. The development of additional diagnostic tests and testing of 91 sera are described in the Final Analysis section of this addendum.

Field Station Update: The Lassa Fever Research Project (LFRP) has been disrupted since April 1991, when Liberian rebels invaded the Eastern Province where the LFRP field station is located. The entire project headquarters and hospital base have been relocated to Panguma Hospital, Panguma, Sierra Leone.

Since the relocation, no Lassa fever research or treatment has been carried out in the Nixon Memorial Hospital in Segbwema. Patients are now referred to Panguma Hospital. Lassa fever is the first and second most common cause of death respectively in the male and female wards, and accounts for 17% of all deaths in these two wards. (See attached graphs.)

Panguma Hospital has also been disrupted by rebel activity and a change of government resulting from a successful coup. In December 1993, the Panguma Hospital closed its inpatient facilities because of new rebel activity. To avoid the insurgence, the LFRP project personnel are now conducting a study outside of the Eastern Province to determine the prevalence of Lassa antibody and antigen in the general population. The project remains without a clinical director because of the continued political unrest.

The following is a summary of the investigations of suspect Lassa fever cases completed since submission of the May 1992 report.

1 RESEARCH ON CLINICAL FEATURES, IMMUNE RESPONSES, AND PATHOPHYSIOLOGY: No additional research has been completed.

2 RESEARCH ON PERSON-TO-PERSON AND HOUSEHOLD TRANSMISSION: No additional research has been completed.

3 RESEARCH ON IMPROVED METHODS FOR EARLY RAPID DIAGNOSIS: The IgM-capture enzyme-linked immunosorbent assay (ELISA) has been assembled and the 91 patients from the reporting period (April 11, 1991 to February 25, 1992) have been tested. IgM-capture ELISA antibody appeared earlier than the IgG or IgM immunofluorescent antibody (IFA) in 4 of 13 patients who tested positive for the IgM and IFA test.

The attached tables show the comparison of results from the IFA test, the IgM-capture ELISA, and the antigen-capture ELISA. (Attachments 1-3)

Results of the antigen-capture ELISA were compared with those of virus isolation for 20 patients; of those who were positive by the antigen-capture ELISA, only 2 were positive by virus isolation (Attachment 4). This finding has important implications for assessment of early deaths and for the confirmation of specimens arriving from the field without proper handling for isolation.

The IgG IFA test has now been used on 2,500 survey samples and has the advantage of longevity as described in the previous report.

4 DIAGNOSIS OF OTHER ETIOLOGIES OF LASSA FEVER LIKE ILLNESS IN SIERRA LEONE: Of the 91 cases evaulated during this reporting period, 44 were identified as non-Lassa illnesses. These 44 specimens were tested by using the IFA technique for CCHF, LCM, Rift Valley fever, Ebola, and yellow fever, and none were positive for other viral antibodies.

These specimens are available for testing by USAMDOC as described in the previous report.

5 REDEFINITION OF EPIDEMIC CHARACTERISTICS OF LASSA VIRUS INFECTIONS IN SIERRA LEONE:

a. Prospective survey of village populations: No studies have been carried out because of the lack of a clinical director and the unstable political situation.

b. Epidemiology in other regions: All studies were described in the previous report.

6 FINAL ANALYSIS

The antigen detection ELISA showed positive results for 27 (57%) of 47 Lassa fever cases. This test provides the ability to confirm the presence of viral antigen in patients within 2 days of admission and such results are important for determining the need for early treatment of patients with ribavirin described in the May 1992 report. The analysis also shows that death due to Lassa fever is highly associated with antigen-positive status, and the test therefore (83%) may be a good predictor of mortality or severity of disease.

The newly developed IgM-capture ELISA, which confirmed 39 (83%) of 47 cases within 4 days of admission, is also an important indicator of the early treatment of patients. The most significant finding of the analysis was observed with the combined use of IgM-capture ELISA and the antigen-detection ELISA. This combination was able to detect 100% of confirmed cases, 90% of which were detected within 4 days of admission.

Furthermore, both the IgM-capture and antigen-detection ELISAs are readily usable in field laboratories such as the Panguma Hospital or Kenema laboratory. The use of this combination of tests in the field has the potential to increase the rapid diagnosis of all cases by as much as 71% in the Sierra Leone field station.

The results of this study show that it is possible to decrease the time required to diagnose Lassa fever, improve the diagnosis of disease among early deaths for which seroconversion cannot be demonstrated, and determine the need for earlier administration of ribavirin to Lassa cases. The use of these test results will also help reduce the administration of ribavirin to non-Lassa cases, which is important in a country such as Sierra Leone where resources for health care are limited.

Lassa IgM

	IgM		
Lassa Case	Negative	Positive	Total
Not a Case	40	4	44
Case	8	39	47
Total	48	43	91

CDC - DVRD

IFAT Compared to IgM and Antigen ELISA

	IFAT		
Antigen or IgM	Negative	Positive	Total
Negative	39	2	41
Positive	20	33	53
Total	59	35	94

CDC - DVRD

Lassa IFAT Seroconversion or High Initial Titer

	IFAT Status		
Lassa Case	Negative	Positive	Total
Not a Case	42	2	44
Case	15	32	47
Total	57	34	91

CDC - DVRD

Isolation and Antigen Detection in Liver Tissue of Fatal Lassa Cases

	Isolation		
Antigen	Negative	Positive	Total
Negative	7	0	7
Positive	11	2	13
Total	18	2	20

CDC - DVRD

Antigen Detection Among Lassa Cases Only

	Lassa Antigen		
Death	Negative	Positive	Total
No	20	13	33
Yes	0	14	14
Total	20	27	47

RR = 2.07 (1.40-3.07)

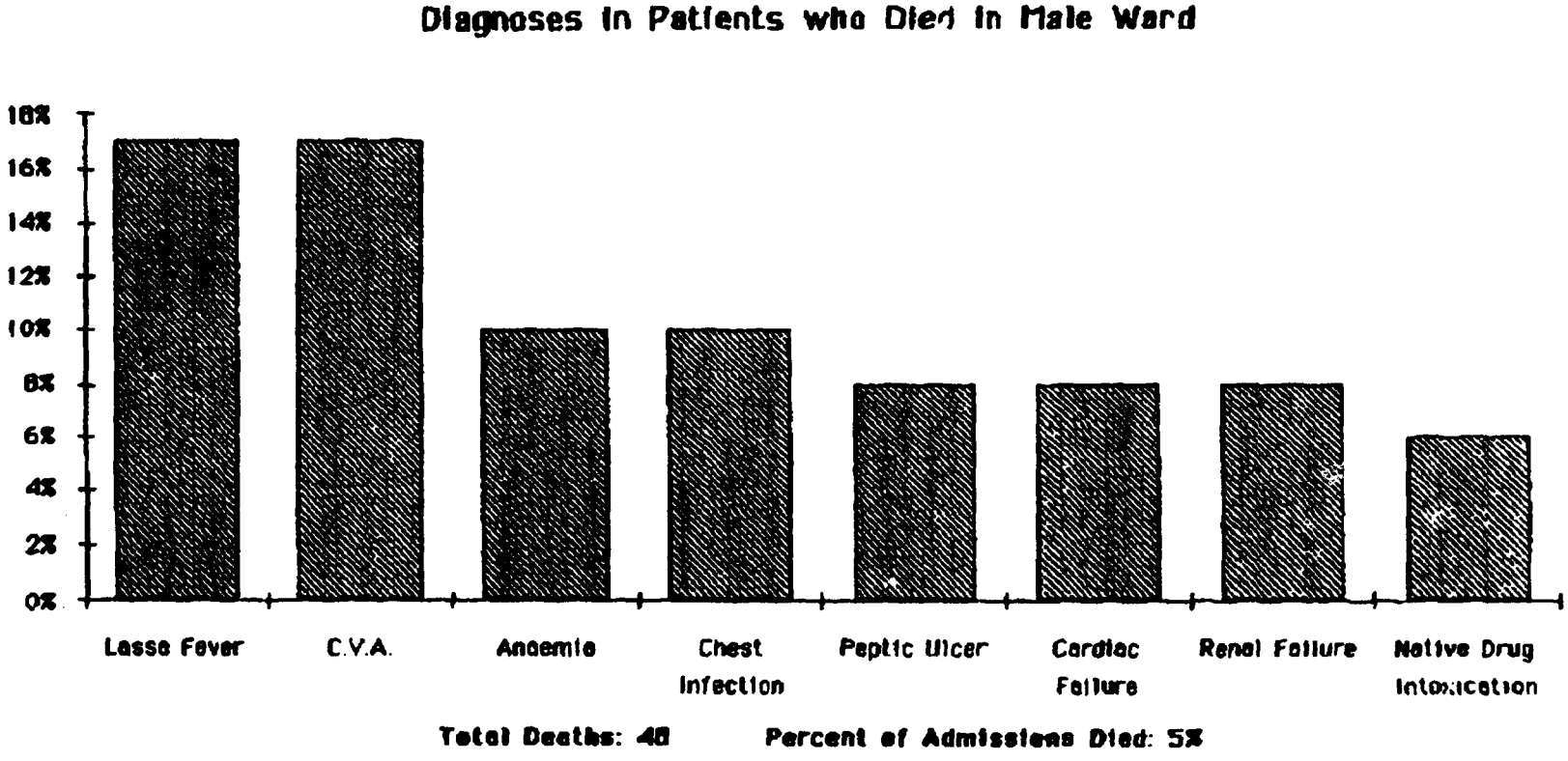
CDC - DVRD

Lassa Antigen Detection

	Lassa Antigen		
Lassa Case	Negative	Positive	Total
No	41	3	44
Yes	20	27	47
Total	61	30	91

CDC - DVRD

APPENDIX D (i)


Diagnoses in Patients who Died in Male Ward
18%
16%
14%
12%
10%
8%
6%
4%
2%
0%
Lassa Fever
C.V.A.
Anaemia
Chest Infection
Peptic Ulcer
Cardiac Failure
Renal Failure
Native Drug Intoxication
Total Deaths: 48
Percent of Admissions Died: 5%

APPENDIX D (ii)